

## Additional file 1

**Supplementary methods and tables for:** Pani L, Tascadda F. AI-assisted characterization of psychedelic clinical trials from ClinicalTrials.gov. *Trials* (revised submission, September 2026).

Contents: Section S1, first-stage AI-assisted extraction workflow and prompts. Section S2, extraction and coding schema. Section S3, second-stage query protocol. Table S1, search terms by compound. Table S2, biomarker assessments in exploratory studies. Table S3, query expressions and returned counts for every figure reported in the manuscript.

### Section S1. First-stage AI-assisted extraction workflow and prompts (13 January 2026)

#### S1.1 System and access

Model: Claude Opus 4.5 (Anthropic), accessed through the Claude web application (claude.ai) with default settings. Registry access: the ClinicalTrials.gov Model Context Protocol (MCP) connector, which exposes the public ClinicalTrials.gov API version 2 (<https://clinicaltrials.gov/data-api/api>) to the model as a set of read-only search and retrieval tools. Every registry search in this stage was executed as a live API call; the returned JSON records (title, sponsor, phase, status, conditions, interventions, enrollment, locations, eligibility criteria, outcome measures) were displayed in the interface and used by the model to compose its summaries. No fine-tuning, no additional data sources and no custom code were used. Date of session: 13 January 2026.

#### S1.2 Workflow

- Step 1 — Landscape queries. The first author asked the model, in natural language, to identify all interventional trials of each compound and to summarize the number of trials by indication. The model chose its own search terms, paginated through results and reported approximate totals.
- Step 2 — Focused retrieval. For psilocybin trials in depression, the model was asked to retrieve phase 2 and phase 3 trials and to tabulate primary and secondary outcome measures, time frames, comparator arms, eligibility criteria, dosing and safety assessments (the content of Tables 4–10 of the main text).
- Step 3 — Cross-compound comparison. The model was asked to compare dosing, session structure and safety monitoring across compounds and to identify the largest late-phase trial of each.
- Step 4 — Verification. The first author checked the trials named in the drafted tables against their registry pages.

Because the counts obtained in this stage were approximate and were later found to underestimate the registry record (main text, Discussion), all counts in the revised manuscript come from the second-stage protocol (Section S3). The first stage remains the source of the qualitative content of Tables 5, 6 and 8–10.

#### S1.3 Prompts

The prompts below are reproduced from the session log.

```
Prompt 1 (landscape): "Using the ClinicalTrials.gov connector, search for all interventional clinical trials of psilocybin, MDMA, LSD, DMT, 5-MeO-DMT, ayahuasca,
```

ibogaine, ketamine and esketamine registered through today. For each compound report the number of trials and the main indications (depression, PTSD, addiction, anxiety, other)."

Prompt 2 (endpoints): "Retrieve the phase 2 and phase 3 trials of psilocybin for depression. For each, extract the primary outcome measure and time frame, secondary outcome measures, comparator arms, dose, and eligibility criteria (age limits, diagnostic confirmation, severity threshold, treatment resistance, key exclusions, prior psychedelic use). Summarize the most common instruments, definitions of response and remission, and assessment time points in tables."

Prompt 3 (comparison): "Compare dosing, session structure and safety monitoring across the compounds, and identify the largest late-phase trial of each compound with its NCT number, sponsor, enrollment and number of sites."

## Section S2. Extraction and coding schema

Structured fields taken directly from the API output: NCT number; title; lead sponsor and sponsor class; phase; study type; overall status; healthy-volunteer flag; enrollment (planned or actual); number of sites and location countries; registered conditions; interventions and arms; masking; primary and secondary outcome measures with time frames; minimum and maximum age. Free-text fields used for the first-stage characterization: eligibility criteria; brief and detailed descriptions; intervention descriptions; outcome descriptions.

Categories used in the tables: (a) compound (psilocybin; MDMA; LSD; DMT/5-MeO-DMT; ayahuasca; ibogaine; ketamine/esketamine); (b) population (patient trials, healthy-volunteer flag = no; healthy-volunteer or mixed studies, flag = yes); (c) indication by registered condition (depression, including bipolar depression only when 'depression' appears in the condition; PTSD; substance use disorder; anxiety; other); (d) phase as registered (phase 2/3 set = phase 2, phase 2/3 or phase 3); (e) primary outcome instrument by name in the primary outcome measure field; (f) comparator by name in the intervention, arm or intervention-description fields; (g) eligibility criterion by term in the eligibility-criteria text; (h) geography by location country; (i) sponsor class as registered (industry; NIH, other federal or other government; other, i.e., academic, hospital, non-profit or individual).

## Section S3. Second-stage query protocol (4 September 2026)

Model: Claude Fable 5.1 (Anthropic) accessed as in S1.1 with the same ClinicalTrials.gov MCP connector (API version 2). Each count was obtained from a single call to the connector's search tool with the 'count total' option, which returns the number of records matching the query. Queries were composed by the model at the first author's direction and are reproduced verbatim in Table S3.

### S3.1 Query structure

Each call combined an intervention term set (passed to the API's query.intr parameter, which searches intervention names, other names and arm-group intervention names with automatic synonym expansion) with an advanced filter in Essie expression syntax (passed to the API's filter.advanced parameter). Every advanced filter begins with the base filter:

```
BASE = AREA[StudyType]INTERVENTIONAL AND AREA[StudyFirstPostDate]RANGE[MIN,2026-01-13] AND NOT AREA[OverallStatus]WITHDRAWN
```

Trials in patient populations add the healthy-volunteer flag:

```
PAT = AREA[HealthyVolunteers]false
```

### Intervention term sets:

PSI = psilocybin OR psilocin OR COMP360 OR CYB003 OR PEX010  
MDMA = MDMA OR midomafetamine OR methylenedioxymethamphetamine  
LSD = lysergic OR lysergide OR MM120 OR MM-120 OR LSD-25  
DMT = dimethyltryptamine OR 5-MeO-DMT OR mebufotenin OR GH001 OR GH002 OR SPL026  
OR CYB004 OR BPL-003 OR "N,N-DMT"  
AYIB = ayahuasca OR ibogaine OR noribogaine  
CORE = PSI OR MDMA OR LSD OR DMT OR AYIB (all terms joined with OR in one query.intr string)  
KET = ketamine OR esketamine OR Spravato OR arketamine

### Registered-condition term sets (Essie, AREA[Condition]):

DEP = AREA[Condition](depression OR depressive OR depressed OR dysthymia OR "mood disorder")  
PTSD = AREA[Condition](PTSD OR "post-traumatic" OR posttraumatic OR "post traumatic")  
SUD = AREA[Condition]("substance use" OR "alcohol use" OR "opioid use" OR "tobacco use" OR "cannabis use" OR "cocaine use" OR "methamphetamine use" OR addiction OR alcoholism OR dependence OR smoking OR nicotine OR "substance abuse" OR "drug use" OR "substance-related" OR "alcohol-related" OR "amphetamine-related")  
ANX = AREA[Condition](anxiety)  
OTHER = NOT AREA[Condition](<all DEP, PTSD, SUD and ANX terms>)  
PSY = AREA[Condition](depression OR depressive OR depressed OR dysthymia OR "mood disorder" OR bipolar OR PTSD OR "post-traumatic" OR posttraumatic OR "post traumatic" OR anxiety OR obsessive OR OCD OR "substance use" OR "alcohol use" OR "opioid use" OR "cocaine use" OR "cannabis use" OR "tobacco use" OR addiction OR alcoholism OR "substance-related" OR "alcohol-related" OR suicidal OR suicide OR suicidality OR anorexia OR bulimia OR "eating disorder")  
KEX = NOT AREA[Condition]("respiratory depression" OR anesthesia OR anaesthesia OR sedation OR "postoperative" OR "post-operative" OR surgery OR surgical OR analgesia OR electroconvulsive OR ECT OR "spreading depression")  
PH23 = AREA[Phase](PHASE2 OR PHASE3)  
DEPSET = BASE AND PAT AND DEP AND PH23, with query.intr = PSI (the phase 2/3 psilocybin-for-depression set, n = 63)

## S3.2 False-positive handling

Retrieved records were listed and reviewed whenever a term set was suspected of matching unrelated records. (i) The bare term 'LSD' retrieved 59 records, of which 17 were unrelated (lysosomal storage diseases, low-starch diet, long slow distance training, and others; Table S3, Q3b); LSD was therefore searched with the specific terms above, and the 4 unrelated records that these still retrieved (NCT01045460, NCT00566098, NCT03207165, NCT00314340) were removed from every LSD and core-set count, 3 of them from patient-trial counts. (ii) 'dimethyltryptamine' matched the chemical name of psilocybin; the 13 psilocybin-only records retrieved by the DMT term set (NCT05301608, NCT02950467, NCT00465595, NCT05065294, NCT04932434, NCT00302744, NCT00957359, NCT06258031, NCT04620759, NCT05351541, NCT01943994, NCT02145091, NCT06455293) were removed from the DMT count; for patient-trial and indication counts the DMT term set was combined with NOT psilocybin. (iii) Two DMT-plus-harmine records and one oral DMT-analogue record retrieved by the ayahuasca/ibogaine term set were counted in the DMT set only.

### S3.3 Counting conventions

- Indication and criterion columns are not mutually exclusive; 'Other' is the count of trials matching none of the four named indication term sets.
- For LSD, DMT/5-MeO-DMT, ayahuasca and ibogaine, whose patient-trial sets contain 3–13 records, indications were assigned by reading the registered conditions of each retrieved record (listed in Table S3) rather than by separate queries.
- Time-frame windows count trials whose primary outcome time frame names any time point in the window; a trial can contribute to more than one window.
- Eligibility-criterion frequencies count trials whose eligibility-criteria text contains any of the listed terms; the direction of the criterion (inclusion or exclusion) is not inferred.
- Geography counts trials with at least one site in the region; multinational trials count in each region. Low- and middle-income countries follow the World Bank classification (Brazil and Pakistan among the countries retrieved).
- Enrollment and site counts in Tables 2 and 3 are the values displayed by the API on 4 September 2026 for the records concerned.

**Table S1. Search terms by compound**

| Compound              | Terms in query.intr (automatic synonym expansion applies)                                    | Known false positives and handling                                                                            |
|-----------------------|----------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------|
| Psilocybin            | psilocybin; psilocin; COMP360; CYB003; PEX010                                                | None identified                                                                                               |
| MDMA                  | MDMA; midomafetamine; methylenedioxymethamphetamine                                          | None identified                                                                                               |
| LSD                   | lysergic; lysergide; MM120; MM-120; LSD-25 (bare 'LSD' not used)                             | 4 unrelated records removed by review                                                                         |
| DMT / 5-MeO-DMT       | dimethyltryptamine; 5-MeO-DMT; mebufotenin; GH001; GH002; SPL026; CYB004; BPL-003; "N,N-DMT" | 13 psilocybin-only records removed (chemical-name match)                                                      |
| Ayahuasca             | ayahuasca                                                                                    | DMT+harmine records assigned to DMT set                                                                       |
| Ibogaine              | ibogaine; noribogaine                                                                        | None identified                                                                                               |
| Ketamine / esketamine | ketamine; esketamine; Spravato; arketamine — restricted to PAT AND PSY AND KEX               | Registered-condition exclusions for anaesthesia, sedation, surgery, analgesia, ECT and respiratory depression |

**Table S2. Biomarker assessments in exploratory studies (first-stage characterization)**

| Biomarker                                        | Rationale                                    | Timing                   |
|--------------------------------------------------|----------------------------------------------|--------------------------|
| Brain-derived neurotrophic factor (BDNF)         | Neuroplasticity marker                       | Baseline; 24 h; week 1   |
| Inflammatory markers (IL-6, TNF- $\alpha$ , CRP) | Inflammation hypothesis of depression        | Baseline; post-dose      |
| Cortisol                                         | Hypothalamic–pituitary–adrenal axis function | Baseline; during session |
| Functional MRI (resting state and task-based)    | Network connectivity                         | Baseline; 1 day; 1 week  |
| Electroencephalography                           | Neural oscillations                          | During dosing session    |
| Genetic markers (5-HTTLPR, CYP2D6)               | Pharmacogenomic prediction                   | Baseline                 |

**Table S3. Query expressions and returned counts for every figure reported in the manuscript**

Executed 4 September 2026 through the ClinicalTrials.gov MCP connector (API v2, search endpoint, count-total option). 'Intr' is the query.intr term set (Section S3.1); 'Advanced filter' is the Essie expression passed as filter.advanced, with BASE and the other abbreviations defined in Section S3.1. 'Returned' is the total reported by the API; 'Reported' is the figure used in the manuscript after the adjustments noted.

| ID  | Figure                             | Intr                                                         | Advanced filter                                                                                                                                    | Returned | Reported / notes                                                   |
|-----|------------------------------------|--------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|----------|--------------------------------------------------------------------|
| Q1  | Psilocybin, all trials             | PSI                                                          | BASE                                                                                                                                               | 244      | 244                                                                |
| Q2  | MDMA, all trials                   | MDMA                                                         | BASE                                                                                                                                               | 99       | 99                                                                 |
| Q3  | LSD, all trials                    | LSD                                                          | BASE                                                                                                                                               | 43       | 39 (4 unrelated records removed)                                   |
| Q3b | Check of the bare term             | LSD NOT (lysergic OR lysergide OR MM120 OR MM-120 OR LSD-25) | BASE                                                                                                                                               | 17       | All 17 unrelated; bare term abandoned                              |
| Q4  | DMT/5-MeO-DMT, all trials          | DMT                                                          | BASE                                                                                                                                               | 49       | 36 (13 psilocybin-only records removed)                            |
| Q5  | Ayahuasca and ibogaine, all trials | AYIB                                                         | BASE                                                                                                                                               | 13       | Ayahuasca 6; ibogaine/noribogaine 4; 3 records assigned to DMT set |
| Q6  | Core set, unique trials            | CORE                                                         | BASE                                                                                                                                               | 416      | 412 (4 unrelated LSD records removed)                              |
| Q7  | Core set, patient trials           | CORE                                                         | BASE AND PAT                                                                                                                                       | 259      | 256 (3 unrelated records removed)                                  |
| Q8  | Psilocybin, patient trials         | PSI                                                          | BASE AND PAT                                                                                                                                       | 181      | 181                                                                |
| Q9  | Psilocybin, depression             | PSI                                                          | BASE AND PAT AND DEP                                                                                                                               | 74       | 74                                                                 |
| Q10 | Psilocybin, PTSD                   | PSI                                                          | BASE AND PAT AND PTSD                                                                                                                              | 17       | 17                                                                 |
| Q11 | Psilocybin, substance use          | PSI                                                          | BASE AND PAT AND SUD                                                                                                                               | 30       | 30                                                                 |
| Q12 | Psilocybin, anxiety                | PSI                                                          | BASE AND PAT AND ANX                                                                                                                               | 12       | 12                                                                 |
| Q13 | Psilocybin, other                  | PSI                                                          | BASE AND PAT AND OTHER                                                                                                                             | 64       | 64                                                                 |
| Q14 | Psilocybin, cancer/palliative      | PSI                                                          | BASE AND PAT AND AREA[Condition](cancer OR neoplasm OR palliative OR "end of life" OR demoralization OR terminal OR hospice OR "life-threatening") | 21       | 21                                                                 |
| Q15 | Psilocybin, OCD/BDD                | PSI                                                          | BASE AND PAT AND AREA[Condition]("obsessive" OR OCD OR "body dysmorphic")                                                                          | 9        | 9                                                                  |
| Q16 | Psilocybin, eating disorders       | PSI                                                          | BASE AND PAT AND AREA[Condition](anorexia OR bulimia OR "binge eating" OR "eating disorder")                                                       | 7        | 7                                                                  |
| Q17 | Psilocybin, pain/headache          | PSI                                                          | BASE AND PAT AND AREA[Condition](pain OR headache OR migraine OR fibromyalgia OR neuralgiform OR neuropathy)                                       | 20       | 20                                                                 |
| Q18 | MDMA, patient trials               | MDMA                                                         | BASE AND PAT                                                                                                                                       | 47       | 47                                                                 |

| ID  | Figure                                            | Intr                   | Advanced filter                                                                                                                                                                                                                                               | Returned | Reported / notes                                                                                                            |
|-----|---------------------------------------------------|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-----------------------------------------------------------------------------------------------------------------------------|
| Q19 | MDMA, PTSD                                        | MDMA                   | BASE AND PAT AND PTSD                                                                                                                                                                                                                                         | 35       | 35                                                                                                                          |
| Q20 | MDMA, substance use                               | MDMA                   | BASE AND PAT AND SUD                                                                                                                                                                                                                                          | 5        | 5                                                                                                                           |
| Q21 | MDMA, anxiety or depression                       | MDMA                   | BASE AND PAT AND AREA[Condition](anxiety OR depression OR depressive OR depressed OR dysthymia OR "mood disorder")                                                                                                                                            | 3        | Anxiety 3; depression 0 (records reviewed)                                                                                  |
| Q22 | MDMA, other                                       | MDMA                   | BASE AND PAT AND OTHER                                                                                                                                                                                                                                        | 8        | 8                                                                                                                           |
| Q23 | LSD, patient trials                               | LSD                    | BASE AND PAT                                                                                                                                                                                                                                                  | 16       | 13 (3 unrelated removed); indications assigned by reading the 13 records: depression 3, anxiety 6, substance use 1, other 4 |
| Q24 | DMT/5-MeO-DMT, patient trials                     | (DMT) NOT psilocybin   | BASE AND PAT                                                                                                                                                                                                                                                  | 12       | 12; indications by reading the records: depression 8, substance use 2, anxiety 1, other 1                                   |
| Q25 | Ayahuasca and ibogaine, patient trials            | AYIB (records from Q5) | —                                                                                                                                                                                                                                                             | —        | Ayahuasca 4 (depression 2, PTSD 1, other 1); ibogaine 3 (substance use 3), by reading the records                           |
| Q26 | Ketamine/esketamine, psychiatric patient trials   | KET                    | BASE AND PAT AND PSY AND KEX                                                                                                                                                                                                                                  | 300      | 300                                                                                                                         |
| Q27 | Ketamine class, depression/bipolar                | KET                    | BASE AND PAT AND AREA[Condition](depression OR depressive OR depressed OR dysthymia OR "mood disorder" OR bipolar) AND KEX                                                                                                                                    | 237      | 237                                                                                                                         |
| Q28 | Ketamine class, PTSD                              | KET                    | BASE AND PAT AND PTSD AND KEX                                                                                                                                                                                                                                 | 21       | 21                                                                                                                          |
| Q29 | Ketamine class, substance use                     | KET                    | BASE AND PAT AND AREA[Condition]("substance use" OR "alcohol use" OR "opioid use" OR "cocaine use" OR "cannabis use" OR "tobacco use" OR addiction OR alcoholism OR "substance-related" OR "alcohol-related") AND KEX AND NOT AREA[Condition]("chronic pain") | 25       | 25                                                                                                                          |
| Q30 | Ketamine class, anxiety/OCD                       | KET                    | BASE AND PAT AND AREA[Condition](anxiety OR obsessive OR OCD) AND KEX AND NOT AREA[Condition](preoperative OR "pre-operative" OR dental)                                                                                                                      | 23       | 23                                                                                                                          |
| Q31 | Ketamine class, suicidality/eating disorders only | KET                    | BASE AND PAT AND AREA[Condition](suicidal OR suicide OR suicidality OR anorexia OR bulimia OR "eating disorder") AND NOT AREA[Condition](<DEP, bipolar, PTSD, ANX/OCD, SUD terms and KEX terms>)                                                              | 14       | 14                                                                                                                          |
| Q32 | Core set, phase 3 or 2/3                          | CORE                   | BASE AND AREA[Phase]PHASE3                                                                                                                                                                                                                                    | 24       | 24 (psilocybin 13, MDMA 8, LSD 3; records listed and used for Tables 2 and 3)                                               |
| Q33 | Phase 2/3 psilocybin-for-depression set           | PSI                    | DEPSET                                                                                                                                                                                                                                                        | 63       | 63                                                                                                                          |

| ID  | Figure                                    | Intr | Advanced filter                                                                                                                                                                                                                                                                                                                                                                                  | Returned | Reported / notes                                       |
|-----|-------------------------------------------|------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|--------------------------------------------------------|
| Q34 | Primary outcome: MADRS                    | PSI  | DEPSET AND AREA[PrimaryOutcomeMeasure] (MADRS OR Montgomery)                                                                                                                                                                                                                                                                                                                                     | 25       | 25                                                     |
| Q35 | Primary outcome: HAM-D                    | PSI  | DEPSET AND AREA[PrimaryOutcomeMeasure] (HAM-D OR HAMD OR Hamilton OR HDRS OR GRID-HAMD OR HRSD)                                                                                                                                                                                                                                                                                                  | 7        | 7                                                      |
| Q36 | Primary outcome: QIDS                     | PSI  | DEPSET AND AREA[PrimaryOutcomeMeasure] (QIDS OR "Quick Inventory")                                                                                                                                                                                                                                                                                                                               | 4        | 4                                                      |
| Q37 | Primary outcome: BDI, PHQ-9 or CGI        | PSI  | DEPSET AND AREA[PrimaryOutcomeMeasure] (BDI OR Beck OR PHQ OR "Patient Health Questionnaire" OR CGI OR "Clinical Global")                                                                                                                                                                                                                                                                        | 4        | 4                                                      |
| Q38 | Primary outcome: any depression scale     | PSI  | DEPSET AND AREA[PrimaryOutcomeMeasure] (<all Q34-Q37 terms>)                                                                                                                                                                                                                                                                                                                                     | 35       | 35; no symptom-severity primary outcome = 63 – 35 = 28 |
| Q39 | Response defined as $\geq 50\%$ reduction | PSI  | DEPSET AND (AREA[PrimaryOutcomeMeasure] ("50%" OR "50 %" OR "50 percent") OR AREA[PrimaryOutcomeDescription] ("50%" OR "50 %" OR "50 percent"))                                                                                                                                                                                                                                                  | 9        | 9                                                      |
| Q40 | Response or remission named               | PSI  | DEPSET AND (AREA[PrimaryOutcomeMeasure] (remission OR response OR responder) OR AREA[PrimaryOutcomeDescription] (remission OR response OR responder OR "50%"))                                                                                                                                                                                                                                   | 18       | 18                                                     |
| Q41 | Time frame includes weeks 3–6             | PSI  | DEPSET AND AREA[PrimaryOutcomeTimeFrame] ("week 3" OR "week 4" OR "week 5" OR "week 6" OR "3 weeks" OR "4 weeks" OR "5 weeks" OR "6 weeks" OR "day 21" OR "day 22" OR "day 28" OR "day 29" OR "day 42" OR "day 43" OR "21 days" OR "28 days" OR "42 days" OR "43 days" OR "week three" OR "week four" OR "week six" OR "three weeks" OR "four weeks" OR "six weeks" OR "1 month" OR "one month") | 34       | 34                                                     |
| Q42 | Time frame includes week 6                | PSI  | DEPSET AND AREA[PrimaryOutcomeTimeFrame] ("week 6" OR "6 weeks" OR "day 42" OR "day 43" OR "42 days" OR "43 days" OR "week six" OR "six weeks")                                                                                                                                                                                                                                                  | 16       | 16                                                     |
| Q43 | Time frame includes weeks 8–12            | PSI  | DEPSET AND AREA[PrimaryOutcomeTimeFrame] ("week 8" OR "week 12" OR "8 weeks" OR "12 weeks" OR "day 56" OR "day 84" OR "day 85" OR "3 months" OR "three months" OR "eight weeks" OR "twelve weeks" OR "2 months" OR "two months")                                                                                                                                                                 | 12       | 12                                                     |
| Q44 | Time frame includes weeks 1–2             | PSI  | DEPSET AND AREA[PrimaryOutcomeTimeFrame] ("week 1" OR "week 2" OR "1 week" OR "2 weeks" OR "day 7" OR "day 8" OR "day 14" OR "day 15" OR "7 days" OR "14 days" OR "one week" OR "two weeks")                                                                                                                                                                                                     | 11       | 11                                                     |
| Q45 | Upper age limit $\leq 65$ years           | PSI  | DEPSET AND AREA[MaximumAge] RANGE [MIN, 65 Years]                                                                                                                                                                                                                                                                                                                                                | 26       | 26                                                     |
| Q46 | Upper age limit $\leq 64$ years           | PSI  | DEPSET AND AREA[MaximumAge] RANGE [MIN, 64 Years]                                                                                                                                                                                                                                                                                                                                                | 5        | 5; exactly 65 years = 26 – 5 = 21                      |
| Q47 | Upper age limit $\geq 66$ years           | PSI  | DEPSET AND AREA[MaximumAge] RANGE [66 Years, MAX]                                                                                                                                                                                                                                                                                                                                                | 18       | 18; no upper limit = 63 – 26 – 18 = 19                 |
| Q48 | Lower age limit $< 18$ years              | PSI  | DEPSET AND AREA[MinimumAge] RANGE [MIN, 17 Years]                                                                                                                                                                                                                                                                                                                                                | 0        | 0                                                      |
| Q49 | Lower age limit $\geq 19$ years           | PSI  | DEPSET AND AREA[MinimumAge] RANGE [19 Years, MAX]                                                                                                                                                                                                                                                                                                                                                | 19       | 19; lower limit 18 years = 63 – 19 = 44                |

| ID  | Figure                                              | Intr | Advanced filter                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          | Returned | Reported / notes                                                   |
|-----|-----------------------------------------------------|------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|--------------------------------------------------------------------|
| Q50 | Structured diagnostic interview                     | PSI  | DEPSET AND AREA[EligibilityCriteria](SCID OR "M.I.N.I." OR "MINI" OR "structured clinical interview" OR "Mini-International" OR "Mini International" OR "structured diagnostic interview" OR "structured interview")                                                                                                                                                                                                                                                                                                                     | 31       | 31                                                                 |
| Q51 | Severity threshold on a rating scale                | PSI  | DEPSET AND AREA[EligibilityCriteria](MADRS OR Montgomery OR HAM-D OR HAMD OR Hamilton OR HDRS OR HRSD OR QIDS OR PHQ-9 OR BDI OR "Beck Depression")                                                                                                                                                                                                                                                                                                                                                                                      | 34       | 34                                                                 |
| Q52 | Treatment-resistant population                      | PSI  | DEPSET AND (AREA[EligibilityCriteria]("treatment-resistant" OR "treatment resistant" OR "inadequate response" OR "failed to respond" OR "adequate trial" OR "adequate trials" OR "adequate dose" OR "failure of" OR "non-response") OR AREA[Condition]("treatment resistant" OR "treatment-resistant" OR refractory))                                                                                                                                                                                                                    | 31       | 31                                                                 |
| Q53 | ≥2 failed antidepressant trials (broad phrasing)    | PSI  | DEPSET AND AREA[EligibilityCriteria]("two adequate" OR "2 adequate" OR "at least two" OR "at least 2" OR "two or more" OR "2 or more" OR "two failed" OR "2 failed" OR "two antidepressant" OR "2 antidepressant" OR "two prior" OR "2 prior" OR "two previous" OR "2 previous" OR "two different" OR "2 different")                                                                                                                                                                                                                     | 27       | Not used (phrases such as 'at least two' match unrelated criteria) |
| Q54 | ≥2 failed antidepressant trials (specific phrasing) | PSI  | DEPSET AND AREA[EligibilityCriteria]("two adequate" OR "2 adequate" OR "two antidepressant" OR "2 antidepressant" OR "two failed" OR "2 failed" OR "two prior antidepressant" OR "2 prior antidepressant" OR "two or more adequate" OR "2 or more adequate" OR "two or more antidepressant" OR "2 or more antidepressant" OR "at least two antidepressant" OR "at least 2 antidepressant" OR "two pharmacological" OR "2 pharmacological" OR "two previous antidepressant" OR "2 previous antidepressant" OR "two trials" OR "2 trials") | 7        | 7                                                                  |
| Q55 | Psychotic or bipolar disorder                       | PSI  | DEPSET AND AREA[EligibilityCriteria](schizophrenia OR psychotic OR psychosis OR schizoaffective OR bipolar)                                                                                                                                                                                                                                                                                                                                                                                                                              | 61       | 61                                                                 |
| Q56 | Substance use disorder                              | PSI  | DEPSET AND AREA[EligibilityCriteria]("substance use" OR "alcohol use" OR "substance abuse" OR "substance dependence" OR "alcohol dependence" OR "drug abuse" OR "drug dependence" OR "alcohol abuse" OR "substance-related")                                                                                                                                                                                                                                                                                                             | 45       | 45                                                                 |
| Q57 | Suicidality                                         | PSI  | DEPSET AND AREA[EligibilityCriteria](suicidal OR suicide OR suicidality OR C-SSRS OR "Columbia")                                                                                                                                                                                                                                                                                                                                                                                                                                         | 47       | 47                                                                 |
| Q58 | Hypertension                                        | PSI  | DEPSET AND AREA[EligibilityCriteria](hypertension OR hypertensive OR "blood pressure")                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 40       | 40                                                                 |
| Q59 | Cardiovascular disease                              | PSI  | DEPSET AND AREA[EligibilityCriteria](cardiovascular OR cardiac OR "heart disease" OR arrhythmia OR "QTc" OR "QT " OR "myocardial" OR "coronary")                                                                                                                                                                                                                                                                                                                                                                                         | 48       | 48                                                                 |
| Q60 | MAOI use                                            | PSI  | DEPSET AND AREA[EligibilityCriteria](MAOI OR MAOIs OR "monoamine oxidase")                                                                                                                                                                                                                                                                                                                                                                                                                                                               | 18       | 18                                                                 |
| Q61 | Pregnancy or breastfeeding                          | PSI  | DEPSET AND AREA[EligibilityCriteria](pregnant OR pregnancy OR breastfeeding OR "breast-                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 52       | 52                                                                 |

| ID  | Figure                                                        | Intr | Advanced filter                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Returned | Reported / notes                                                                                                                                     |
|-----|---------------------------------------------------------------|------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|------------------------------------------------------------------------------------------------------------------------------------------------------|
|     |                                                               |      | feeding" OR "breast feeding" OR lactating OR lactation OR nursing)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |          |                                                                                                                                                      |
| Q62 | Family history of psychosis                                   | PSI  | DEPSET AND AREA[EligibilityCriteria]("first-degree" OR "first degree" OR "family history")                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 33       | 33                                                                                                                                                   |
| Q63 | Prior psychedelic use                                         | PSI  | DEPSET AND AREA[EligibilityCriteria](psychedelic OR psychedelics OR hallucinogen OR hallucinogens OR "psilocybin use" OR "use of psilocybin")                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   | 38       | 38                                                                                                                                                   |
| Q64 | Niacin or nicotinamide comparator                             | PSI  | DEPSET AND (AREA[InterventionName](niacin OR nicotinamide OR "vitamin B3") OR AREA[ArmGroupInterventionName](niacin OR nicotinamide) OR AREA[InterventionDescription](niacin OR nicotinamide))                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  | 7        | 7                                                                                                                                                    |
| Q65 | Low-dose psilocybin or other active placebo                   | PSI  | DEPSET AND (AREA[InterventionName]("1 mg" OR "1mg" OR "2 mg" OR "2mg" OR "3 mg" OR "5 mg" OR "5mg" OR "low dose" OR "low-dose" OR microdose OR "micro-dose" OR "active placebo" OR "sub-therapeutic" OR subtherapeutic) OR AREA[ArmGroupDescription]("1 mg" OR "1mg" OR "2 mg" OR "3 mg" OR "5 mg" OR "5mg" OR "low dose" OR "low-dose" OR microdose OR "active placebo" OR "sub-therapeutic" OR subtherapeutic OR "very low dose") OR AREA[InterventionDescription]("1 mg" OR "1mg" OR "5 mg" OR "5mg" OR "low dose" OR "low-dose" OR "active placebo" OR "sub-therapeutic" OR subtherapeutic))                                                                                                                                                                                                                                                                                                                | 21       | 21                                                                                                                                                   |
| Q66 | Open-label (no masking)                                       | PSI  | DEPSET AND AREA[DesignMasking]NONE                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | 19       | 19                                                                                                                                                   |
| Q67 | Psychological support described in intervention or arm fields | PSI  | DEPSET AND (AREA[InterventionName](psychotherapy OR "psychological support" OR "psychosocial support" OR "therapeutic support" OR "supportive therapy" OR counseling OR counselling OR "integration" OR "preparation" OR "set and setting" OR "behavioral therapy" OR "behavioural therapy" OR "assisted therapy" OR "assisted psychotherapy") OR AREA[InterventionDescription](psychotherapy OR "psychological support" OR "psychosocial support" OR "integration session" OR "integration sessions" OR "preparatory session" OR "preparatory sessions" OR "preparation session" OR "preparation sessions" OR therapist OR therapists OR facilitator OR facilitators) OR AREA[ArmGroupDescription](psychotherapy OR "psychological support" OR "psychosocial support" OR "integration session" OR "integration sessions" OR "preparatory" OR "preparation session" OR therapist OR therapists OR facilitator)) | 23       | 23                                                                                                                                                   |
| Q68 | Active drug comparators                                       | PSI  | DEPSET AND AREA[InterventionName](escitalopram OR ketamine OR esketamine OR sertraline OR venlafaxine OR risperidone OR midazolam OR "electroconvulsive" OR ECT)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | 5        | Ketamine 2 (NCT03380442, NCT05383313); risperidone 1 mg 2 (NCT05710237, NCT06512220); escitalopram 1 (NCT03429075); midazolam 1 (within NCT05383313) |

| ID  | Figure                                                                       | Intr                      | Advanced filter                                                                                                                                                                                                                                                                                                                                                                                               | Returned | Reported / notes                                                   |
|-----|------------------------------------------------------------------------------|---------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|--------------------------------------------------------------------|
| Q69 | Core patient trials with a North American site                               | CORE                      | BASE AND PAT AND AREA[LocationCountry] ("United States" OR Canada OR Mexico)                                                                                                                                                                                                                                                                                                                                  | 192      | 189 (3 unrelated records removed)                                  |
| Q70 | Core patient trials with a European site                                     | CORE                      | BASE AND PAT AND AREA[LocationCountry] ("United Kingdom" OR Germany OR Switzerland OR Netherlands OR Denmark OR Sweden OR Norway OR Finland OR Ireland OR Spain OR Italy OR France OR Belgium OR Austria OR Portugal OR Poland OR Czechia OR "Czech Republic" OR Hungary OR Greece OR Croatia OR Estonia OR Latvia OR Lithuania OR Slovakia OR Slovenia OR Romania OR Bulgaria OR Iceland OR Luxembourg)      | 57       | 57                                                                 |
| Q71 | Core patient trials with an Australian or New Zealand site                   | CORE                      | BASE AND PAT AND AREA[LocationCountry] (Australia OR "New Zealand")                                                                                                                                                                                                                                                                                                                                           | 5        | 5                                                                  |
| Q72 | Core patient trials with sites outside North America, Europe and Australasia | CORE                      | BASE AND PAT AND AREA[LocationCountry] (Israel OR Brazil OR India OR "South Africa" OR Colombia OR Argentina OR Turkey OR Türkiye OR China OR Thailand OR Iran OR Egypt OR Peru OR Indonesia OR Pakistan OR Nigeria OR Kenya OR Ukraine OR Malaysia OR Vietnam OR Philippines OR Jamaica OR Costa Rica OR Ecuador OR Chile OR Uruguay OR Japan OR "Korea, Republic of" OR Singapore OR Taiwan OR "Hong Kong") | 14       | Israel 9; Brazil 4; Pakistan 1 (records listed and read)           |
| Q73 | Core set, industry lead sponsor                                              | CORE                      | BASE AND AREA[LeadSponsorClass]INDUSTRY                                                                                                                                                                                                                                                                                                                                                                       | 84       | 84                                                                 |
| Q74 | Core set, government lead sponsor                                            | CORE                      | BASE AND AREA[LeadSponsorClass] (NIH OR FED OR OTHER_GOV OR NETWORK)                                                                                                                                                                                                                                                                                                                                          | 12       | 12; other (academic, non-profit, individual) = 412 – 84 – 12 = 316 |
| Q75 | ESCAPE-TRD registry record                                                   | esketamine AND quetiapine | AREA[StudyType]INTERVENTIONAL AND AREA[StudyFirstPostDate]RANGE [MIN, 2026-01-13] AND AREA[Phase]PHASE3                                                                                                                                                                                                                                                                                                       | 2        | NCT04338321: enrollment 676, 171 sites                             |

*Abbreviations as in the main text. Records listed under 'records listed and read' were displayed in full by the connector and classified by reading their registered conditions; the NCT numbers of every analytic set are available from the corresponding author.*